

### Claims

- 1           1. Substantially pure DNA encoding a high-affinity  
2 melatonin receptor.
- 1           2. The DNA of claim 1, wherein said DNA is genomic  
2 DNA.
- 1           3. The DNA of claim 1, wherein said DNA is cDNA.
- 1           4. The DNA of claim 1, wherein said DNA is  
2 mammalian.
- 1           5. Substantially pure DNA having the sequence of  
2 Fig. 1 (SEQ ID NO:1), or degenerate variants thereof, and  
3 encoding the amino acid sequence of Fig. 1 (SEQ ID NO:2).
- 1           6. Substantially pure DNA having the sequence of  
2 Fig. 2 (SEQ ID NO:3), or degenerate variants thereof, and  
3 encoding the amino acid sequence of Fig. 2 (SEQ ID NO:4).
- 1           7. Substantially pure DNA comprising the DNA  
2 sequence of Fig. 4 (SEQ ID NO:5), or degenerate variants  
3 thereof, and encoding an amino acid sequence comprising the  
4 amino acid sequence of Fig. 4 (SEQ ID NO:6).
- 1           8. Substantially pure DNA comprising the DNA  
2 sequence of Fig. 5 (SEQ ID NO:11), or degenerate variants  
3 thereof, and encoding an amino acid sequence comprising the  
4 amino acid sequence of Fig. 5 (SEQ ID NO:12).

1           9. Substantially pure DNA comprising the DNA  
2 sequence of Fig. 3 (SEQ ID NO:13), or degenerate variants  
3 thereof, and encoding an amino acid sequence comprising the  
4 amino acid sequence of Fig. 3 (SEQ ID NO:14).

1           10. Substantially pure DNA comprising the DNA  
2 sequence of Fig. 6 (SEQ ID NO:15), or degenerate variants  
3 thereof, and encoding an amino acid sequence comprising the  
4 amino acid sequence of Fig. 6 (SEQ ID NO:16).

1           11. Substantially pure DNA having 50% or greater  
2 sequence identity to the DNA sequence of Fig. 2 (SEQ ID  
3 NO:3) and encoding a protein capable of binding melatonin.

1           12. Substantially pure DNA which hybridizes to the  
2 DNA sequence of Fig. 1 (SEQ ID NO:1) under conditions of  
3 high stringency.

1           13. Substantially pure DNA which hybridizes to the  
2 DNA sequence of Fig. 2 (SEQ ID NO:3) under conditions of  
3 high stringency.

1           14. Substantially pure DNA which hybridizes to the  
2 DNA sequence of Fig. 4 (SEQ ID NO:5) under conditions of  
3 high stringency.

1           15. Substantially pure DNA which hybridizes to the  
2 DNA sequence of Fig. 5 (SEQ ID NO:11) under conditions of  
3 high stringency.

1           16. Substantially pure DNA which hybridizes to the  
2 DNA sequence of Fig. 3 (SEQ ID NO:13) under conditions of  
3 high stringency.

1           17. Substantially pure DNA which hybridizes to the  
2 DNA sequence of Fig. 6 (SEQ ID NO:15) under conditions of  
3 high stringency.

1           18. Substantially pure high-affinity melatonin  
2 receptor protein.

1           19. The receptor protein of claim 18, having an  
2 amino acid sequence substantially identical to the amino  
3 acid sequence shown in Fig. 1 (SEQ ID NO:2).

1           20. The receptor protein of claim 18, having an  
2 amino acid sequence substantially identical to the amino  
3 acid sequence shown in Fig. 2 (SEQ ID NO:4).

1           21. The receptor protein of claim 18, comprising  
2 the amino acid sequence of Fig. 3 (SEQ ID NO:6).

1           22. The receptor protein of claim 18, having an  
2 amino acid sequence substantially identical to the amino  
3 acid sequence shown in Fig. 4 (SEQ ID NO:12).

1           23. The receptor protein of claim 18, having an  
2 amino acid sequence substantially identical to the amino  
3 acid sequence shown in Fig. 3 (SEQ ID NO:14).

1           24. The receptor protein of claim 14, having an  
2 amino acid sequence substantially identical to the amino  
3 acid sequence shown in Fig. 6 (SEQ ID NO:16).

1           25. A substantially pure polypeptide having an  
2 amino acid sequence which is at least 80% identical to the  
3 amino acid sequence shown in Fig. 1 (SEQ ID NO:2), wherein

4           a) said polypeptide binds melatonin; and

5           b) said polypeptide mediates a decrease in  
6 intracellular cAMP concentration in a cell expressing said  
7 polypeptide on its surface.

1           26. A substantially pure polypeptide having an  
2 amino acid sequence which is at least 80% identical to the  
3 amino acid sequence shown in Fig. 2 (SEQ ID NO:4), wherein

4           a) said polypeptide binds melatonin; and

5           b) said polypeptide mediates a decrease in  
6 intracellular cAMP concentration in a cell expressing said  
7 polypeptide on its surface.

1           27. A substantially pure polypeptide having an  
2 amino acid sequence which is at least 80% identical to the  
3 amino acid sequence shown in Fig. 5 (SEQ ID NO:12), wherein

4           a) said polypeptide binds melatonin; and

5           b) said polypeptide mediates a decrease in  
6 intracellular cAMP concentration in a cell expressing said  
7 polypeptide on its surface.

1           28. A substantially pure polypeptide having an  
2 amino acid sequence which is at least 80% identical to the  
3 amino acid sequence shown in Fig. 3 (SEQ ID NO:14), wherein  
4           a) said polypeptide binds melatonin; and  
5           b) said polypeptide mediates a decrease in  
6 intracellular cAMP concentration in a cell expressing said  
7 polypeptide on its surface.

1           29. A substantially pure polypeptide having an  
2 amino acid sequence which is at least 80% identical to the  
3 amino acid sequence shown in Fig. 6 (SEQ ID NO:16), wherein  
4           a) said polypeptide binds melatonin; and  
5           b) said polypeptide mediates a decrease in  
6 intracellular cAMP concentration in a cell expressing said  
7 polypeptide on its surface.

1           30. A substantially pure polypeptide which is a  
2 fragment or analog of a high-affinity melatonin receptor  
3 comprising a domain capable of binding melatonin and  
4 mediating a decrease in intracellular cAMP concentration.

1           31. A vector comprising the DNA of claim 1.

1           32. A cell which contains the DNA of claim 1.

1           33. A method of testing a candidate compound for  
2 the ability to act as an agonist of a high affinity  
3 melatonin receptor ligand, said method comprising:  
4           a) contacting said candidate compound with a cell  
5 which expresses on its surface a recombinant high-affinity  
6 melatonin receptor protein or melatonin binding fragment or  
7 analog thereof;  
8           b) measuring intracellular cAMP concentration in  
9 said cell; and  
10           c) identifying said candidate compound as an agonist  
11 where said contacting causes a decrease in intracellular  
12 cAMP concentration.

1           34. A method of testing a candidate compound for  
2 the ability to act as an antagonist of a high affinity  
3 melatonin receptor ligand, said method comprising:  
4           a) contacting said candidate compound with a cell  
5 which expresses on its surface a recombinant high-affinity  
6 melatonin receptor protein or melatonin binding fragment or  
7 analog thereof;  
8           b) measuring binding between said receptor protein  
9 and melatonin; and  
10           c) identifying said candidate compound as an  
11 antagonist where said contacting causes a decrease in  
12 binding between said recombinant high-affinity melatonin  
13 receptor protein and melatonin.

1           35. The method of claim 25 or 26, wherein said cell  
2 is a mammalian cell which normally presents substantially no  
3 high-affinity melatonin receptor on its surface.

1           36. A therapeutic composition comprising as an  
2 active ingredient high-affinity melatonin receptor agonist,  
3 said active ingredient being formulated in a  
4 physiologically-acceptable carrier.